

## Paraneoplastic Pemphigus: Oral Involvement as the Sole Manifestation

Sir,

The concept of paraneoplastic pemphigus was first established by Anhalt et al. (1) in 1990, with the recognition of a distinct variant of the pemphigus spectrum associated with malignancy. The reports on paraneoplastic pemphigus have multiplied over the last 5 years, all exhibiting the features of a severe, usually fatal, mucocutaneous disease with unique histological and immunological characteristics. The common histological findings in these patients include dyskeratotic keratinocytes and basal vacuolization, in addition to the invariable suprabasilar acantholysis. The ability of antibodies in the patients' sera to bind to a variety of epithelia and to precipitate a unique complex of four antigens is the hallmark of diagnosis of this recently acknowledged entity (1-6).

We describe a case that shares the immunological and histological characteristics of the reported paraneoplastic pemphigus cases but is unique in its clinical behavior.

### CASE REPORT

A 50-year-old Jewish man of Iranian descent was hospitalized in September 1993 for evaluation of painful oral erosions that interfered with his ability to eat. He had a 10-month history of high-grade non-Hodgkin's lymphoma, with remission believed to be induced by multiple agent chemotherapy consisting of VP16, adriamycin, cytoxan, oncovin, prednisone and bleomycin. The erosions appeared about 3 months after completion of this treatment. Cultures taken by the referring physician for fungal organisms and herpes simplex, and serological tests for herpes virus, were all negative. When treatment with acyclovir, antifungal agents and antibiotics proved ineffective, the patient was hospitalized for further evaluation.

Physical examination at admission revealed severe ulcerations and pseudomembranes involving the tongue, palate, buccal mucosa and lips (Fig. 1). There was no skin eruption and no involvement of other mucous membranes. A solitary enlarged inguinal lymph node was palpated. Results of laboratory studies, including complete blood count and serum chemistry profile, were within normal limits.

A biopsy specimen obtained from the oral mucosa showed suprabasal acantholysis, interface vacuolization and dyskeratotic keratinocytes



Fig. 1. Ulcerations and pseudomembranes involving the tongue, palate, buccal mucosa and lips, as observed on hospitalization.

(Fig. 2). Direct immunofluorescent studies of a perilesional biopsy revealed intercellular IgG deposits, as well as linear deposits of C3 along the basement membrane zone. Indirect immunofluorescence of a sample of the patient's serum demonstrated IgG autoantibodies directed not only to the intercellular substance of stratified squamous epithelium, but also to the intercellular substance of rat bladder transitional cell epithelium. Further immunological and immunoprecipitation studies were not performed at that time and, in view of the patient's deteriorating status and the recurrence of the lymphoma disclosed by bone marrow biopsy, salvage chemotherapy was immediately commenced with cytoxan, adriamycin, oncovin and prednisone. A second remission was accompanied by a striking improvement in the oral lesions. A serum sample obtained at the time of the remission was unfortunately negative on indirect immunofluorescence for anti-intercellular antibodies, probably accounting for the subsequent failure to immunoprecipitate proteins synthesized by keratinocyte cultures.





Fig. 2. Biopsy specimen from the oral mucosa showing suprabasal acantholysis, interface vacuolization and dyskeratotic keratinocytes.

The patient was disease-free for 6 months after initiation of salvage treatment, and was subsequently lost to follow-up.

## DISCUSSION

The clinical, histological and immunological findings in our patient suggest the diagnosis of paraneoplastic pemphigus. While the extent of the clinical involvement is unique, the histological and immunological findings in our patient are identical to those described in paraneoplastic pemphigus, namely, the distinct pattern of immunoreactants intercellularly and along the basement membrane zone on direct immunofluorescence, and the positive staining of urinary bladder transitional epithelium by the patient's serum. Indirect immunofluorescence with urinary bladder epithelium was found to be a reasonably specific test, albeit not a very sensitive one (6). Regrettably, immunoprecipitation studies, the hallmark of diagnosis, were not carried out prior to salvage chemotherapy, when autoantibodies were detectable in the serum.

Although the first cases of this rare entity were described by Anhalt et al. (1) in 1990, the full spectrum of the disease remains to be defined. All cases reported to date (5) exhibit a polymorphous skin eruption together with severe mucosal involvement. Our patient is remarkable for the absence of skin lesions throughout the course of the disease, and restriction of lesions to the oral mucosa.

A case of a long-term survivor with extensive mucosal and limited cutaneous lesions was recently described (2). The description of a mucocutaneous disease was applicable in this patient with chronic lymphocytic leukemia who had pemphigus lesions in several mucous membranes (oral, pharyngeal, corneal, conjunctival) along with involvement of the glans penis. Our patient, in contrast, had only mucosal lesions confined to

the mouth. Repeated courses of chemotherapy for chronic lymphocytic leukemia in the above reported patient (2) did not lead to remission of his pemphigus lesions. In our patient, the biological behavior of the mucosal disease closely followed that of his lymphoma: the appearance of the oral erosions signaled the relapse, and aggressive salvage chemotherapy that induced a second remission was promptly followed by clearing of the pemphigus lesions. In previously reported cases the course of the blistering eruption usually did not parallel the course of the underlying causes, and paraneoplastic pemphigus even occurred in a patient apparently cured of the neoplastic disease (3).

The present report indicates that paraneoplastic pemphigus has a more variable clinical involvement than previously believed. The affliction may be extensive and severe, as in the cases described by Anhalt et al. (1), or mild and without cutaneous lesions, as in our case. The progress may vary as well. Although usually rapidly fatal, a subgroup of patients may survive the disease for longer periods of time. Camisa et al. (4) reported a patient still alive and well at 2-year follow-up; Perniciaro et al. (2) described a patient followed by the Mayo Clinic who lived for more than 7 years; and our patient has been disease-free for 6 months. Thus, paraneoplastic pemphigus exhibits not only a broader spectrum of morbidity, but of outcome as well. Awareness of this fact will prevent mild cases from escaping diagnosis, particularly in patients in whom the mucocutaneous lesions precede the detection or a relapse of a neoplastic disease.

## REFERENCES

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